Corrigenda

WHO Classification of Tumours, 5th edition: Soft Tissue and Bone Tumours

November 2022 (for 3rd print run)

Updated corrigenda for this volume can be found at https://publications.iarc.who.int/Book-And-Report-Series/Who-Iarc-Classification-Of-Tumours/Soft-Tissue-And-Bone-Tumours-2020.

Summary of corrections:

The WHO Classification of Tumours Editorial Board (p. iv)

Drs Gronchi and Messiou have been added to the list of WHO Classification of Tumours Editorial Board expert members:

Gronchi, Alessandro
Fondazione IRCCS Istituto Nazionale dei Tumori
Milan

Messiou, Christina
Royal Marsden Hospital
London

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WHO classification of soft tissue tumours: ICD-O coding (p. 2–3)

The following footnote has been added at the end of the WHO classification (ICD-O coding) table:

Subtype labels are indented.

And several ICD-O labels have been corrected as shown below.

Original text	Corrected text
Fibroblastic and myofibroblastic tumours … 9160/0 Angiofibroma NOS	**Fibroblastic and myofibroblastic tumours** … 9160/0 Angiofibroma
So-called fibrohistiocytic tumours … 9251/1 Giant cell tumour of soft parts NOS	**So-called fibrohistiocytic tumours** … 9251/1 Giant cell tumour of soft parts
Peripheral nerve sheath tumours … 9540/3 Melanotic malignant peripheral nerve sheath tumour	**Peripheral nerve sheath tumours** … 9540/3 Malignant melanotic nerve sheath tumour

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Myositis ossificans and fibro-osseous pseudotumour of digits (p. 54)

Text that had accidentally been deleted from this page during the layout process for print has been added back to this section.

A corrected, printable version of page 54 is included at the end of this corrigenda document.

Original text	Corrected text
is extraskeletal osteosarcoma, which lacks zonation and shows malignant cytology. **Cytology** Cytology features …	**Etiology** Unknown **Pathogenesis** Most cases of myositis ossificans and FP harbour the fusion *COL1A1-USP6* (2980,3008,1036,260, 1504). *USP6* fusion genes are also encountered in aneurysmal bone cyst and nodular fasciitis, tumours with overlapping morphology. **Macroscopic appearance** Myositis ossificans is well delineated and ovoid, has a glistening soft-tan haemorrhagic centre and a firm greyish-white gritty periphery, and is 2–12 cm (average: 5 cm). FP is tan/grey/pink, smaller, and less well demarcated. **Histopathology** Myositis ossificans is characterized by zonal architecture. Initially, it is densely cellular, composed of spindle cells oriented randomly or in short intersecting fascicles. The spindle cells have eosinophilic cytoplasm and plump vesicular nuclei with nucleoli. Normal mitoses are often numerous. The stroma is vascular and myxoid and contains fibrin, extravasated erythrocytes, scattered lymphocytes, and osteoclast-like giant cells. Blood-filled cysts may be present. Peripherally, the spindle cells merge with osteoblasts that rim and populate ill-defined trabeculae and sheets of unmineralized woven bone, which is surrounded by well-formed trabecular and cortical-type bone that remodels into lamellar bone. Occasionally, the matrix contains cellular hyaline cartilage or the zonal architecture is not well developed (12,802,2116, 2335,2658,2987). The bone is randomly distributed in FP. An important differential diagnosis is extraskeletal osteosarcoma, which lacks zonation and shows malignant cytology. **Cytology** Cytology features …

Updated online: n/a – This error was present in the print version only
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Angiofibroma of soft tissue (p. 82)

The ICD-O label has been corrected as shown.

Original text	Corrected text
ICD-O coding 9160/0 Angiofibroma NOS	**ICD-O coding** 9160/0 Angiofibroma

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Giant cell tumour of soft tissue (p. 141)

The ICD-O label has been corrected as shown.

Original text	Corrected text
ICD-O coding 9251/1 Giant cell tumour of soft parts NOS	**ICD-O coding** 9251/1 Giant cell tumour of soft parts

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Arteriovenous malformation/haemangioma (p. 147)

Some of the content has been moved from the *Definition* subsection to later in the section as shown below.

Original text	Corrected text
Definition Arteriovenous malformation/haemangioma (AVM/H) is a fast-flow, mostly congenital vascular anomaly characterized by the presence of arteriovenous shunts. There are two distinctive forms: deep-seated and cutaneous (cirsoid aneurysm or acral arteriovenous tumour). Most cases of extracranial AVM/H harbour *MAP2K1* mutations, resulting in upregulated MAP2K1 (MEK1) activity. When these lesions involve multiple tissue planes, they are termed angiomatosis.	**Definition** Arteriovenous malformation/haemangioma (AVM/H) is a fast-flow, mostly congenital vascular anomaly characterized by the presence of arteriovenous shunts.
Subtype(s) None	**Subtype(s)** Deep-seated AVM/H; cutaneous AVM/H (also called cirsoid aneurysm or acral arteriovenous tumour); angiomatosis (involving multiple tissue planes)
Etiology Unknown	**Etiology** Most are solitary and sporadic. Inherited lesions occurring as part of the rare capillary malformation–AVM syndrome are associated with germline *RASA1* mutations, which are probably causative {3064A}.

Original text	Corrected text
Pathogenesis Unknown	**Pathogenesis** Most cases of extracranial AVM/H harbour *MAP2K1* mutations, resulting in upregulated MAP2K1 (MEK1) activity.
Reference cited above: **3064A.** Thiex R, Mulliken JB, Revencu N, et al. A novel association between RASA1 mutations and spinal arteriovenous anomalies. AJNR Am J Neuroradiol. 2010 Apr;31(4):775–9. PMID:20007727	

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Pseudomyogenic haemangioendothelioma (p. 169)

The text has been corrected as shown.

Original text	Corrected text
Related terminology *Acceptable:* epithelioid sarcoma–like haemangioendothelioma.	**Related terminology** *Not recommended:* epithelioid sarcoma–like haemangioendothelioma.

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Embryonal rhabdomyosarcoma (p. 201)

The text has been corrected as shown.

Original text	Corrected text
Subtype(s) Embryonal rhabdomyosarcoma, pleomorphic	**Subtype(s)** Embryonal rhabdomyosarcoma, anaplastic

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Schwannoma (p. 226)

The text has been corrected as shown.

Original text	Corrected text
Related terminology *Acceptable:* neurilemmoma.	**Related terminology** *Not recommended:* neurilemmoma.

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Malignant peripheral nerve sheath tumour (p. 256)

In Table 1.04 (Table #5193 online), in the row for ANNUBP (atypical neurofibromatous neoplasm of uncertain biological potential), the proposed definition has been corrected as shown, in order to provide a lower limit as well as an upper limit.

Original text	Corrected text
ANNUBP: Proposed definition Schwann cell neoplasm with ≥ 2 of the following 4 features: cytological atypia, loss of neurofibroma architecture, hypercellularity, and < 1.5 mitoses/mm^2 (< 3 mitotic figures per 10 HPFs[a])	**ANNUBP: Proposed definition** Schwann cell neoplasm with ≥ 2 of the following 4 features: cytological atypia, loss of neurofibroma architecture, hypercellularity, and a mitotic count of > 0.2 mitoses/mm^2 (> 1 mitotic figure per 50 HPFs[a]) and < 1.5 mitoses/mm^2 (< 3 mitotic figures per 10 HPFs[a])

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Malignant melanotic nerve sheath tumour (p. 258)

The ICD-O label has been corrected as shown.

Original text	Corrected text
ICD-O coding 9540/3 Melanotic malignant peripheral nerve sheath tumour	**ICD-O coding** 9540/3 Malignant melanotic nerve sheath tumour

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Pleomorphic hyalinizing angiectatic tumour of soft parts (p. 280)

The text has been corrected as shown (one term deleted).

Original text	Corrected text
Related terminology *Acceptable:* haemosiderotic fibrolipomatous tumour; early pleomorphic hyalinizing angiectatic tumour.	**Related terminology** *Acceptable:* early pleomorphic hyalinizing angiectatic tumour.

Updated online: Update pending
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WHO classification of bone tumours: ICD-O coding (p. 338)

The following footnote has been added at the end of the WHO classification (ICD-O coding) table:

Subtype labels are indented.

And several ICD-O labels have been corrected as shown below.

Original text	Corrected text
Chondrogenic tumours … 9220/1 Chondromatosis NOS	**Chondrogenic tumours** … 9220/1 Synovial chondromatosis
Osteogenic tumours *Benign* 9180/0 Osteoma NOS 9191/0 Osteoid osteoma NOS	**Osteogenic tumours** *Benign* 9180/0 Osteoma 9191/0 Osteoid osteoma
Osteoclastic giant cell–rich tumours … 9250/1 Giant cell tumour of bone NOS	**Osteoclastic giant cell–rich tumours** … 9250/1 Giant cell tumour of bone
Notochordal tumours … 9370/3 Chordoma NOS	**Notochordal tumours** … 9370/3 Conventional chordoma
Other mesenchymal tumours of bone … 8990/1 Mesenchymoma NOS	**Other mesenchymal tumours of bone** … 8990/1 Fibrocartilaginous mesenchymoma

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WHO classification of bone tumours: ICD-O coding (p. 338)

Under the heading “Haematopoietic neoplasms of bone”, the code has been added for Rosai–Dorfman disease as shown.

Original text	Corrected text
Haematopoietic neoplasms of bone … 9751/1 Langerhans cell histiocytosis NOS 9751/3 Langerhans cell histiocytosis, disseminated 9749/3 Erdheim–Chester disease Rosai–Dorfman disease	**Haematopoietic neoplasms of bone** … 9751/1 Langerhans cell histiocytosis NOS 9751/3 Langerhans cell histiocytosis, disseminated 9749/3 Erdheim–Chester disease 9749/3 Rosai–Dorfman disease

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Chondroblastoma (p. 359–361)

The following subsections have been corrected as shown, to bring the content in line with other volumes and with our 2021 publication on the issue of histone numbering (Leske et al., 2021 – PMID: 33779999).

Original text	Corrected text
Pathogenesis H3.3 alterations are seen in various tumour types including bone tumours like chondroblastoma and giant cell tumour of bone. Specific substitutions are associated with different tumour types: p.Lys36Met with chondroblastoma and p.Gly34Trp with giant cell tumours of bone […]. p.Lys36Met substitutions in chondroblastoma are more frequent in the *H3-3B* (*H3F3B*) gene on chromosome 17 … The p.Lys36Met mutations inhibit the H3K36 methyltransferases NSD2 (MMSET) and SETD2, which results in reduced global H3K36 methylation …	**Pathogenesis** H3.3 alterations are seen in various tumour types including bone tumours like chondroblastoma and giant cell tumour of bone. Specific substitutions are associated with different tumour types: p.K37M (K36M) with chondroblastoma and p.G35W (G34W) with giant cell tumours of bone […]. p.K37M (K36M) substitutions in chondroblastoma are more frequent in the *H3-3B* (*H3F3B*) gene on chromosome 17 … The p.K37M (K36M) alteration inhibits the H3 p.K37 (K36) methyltransferases NSD2 (MMSET) and SETD2, which results in reduced global H3 p.K37 (K36) methylation …
Histopathology … ***Immunohistochemistry*** Immunohistochemistry using an antibody against H3.3B (H3F3B) p.Lys36Met (K36M) shows diffuse nuclear expression …	**Histopathology** … ***Immunohistochemistry*** Immunohistochemistry using an antibody against H3 p.K37M (K36M) shows diffuse nuclear expression …
Diagnostic molecular pathology The vast majority of chondroblastomas harbour a p.Lys36Met substitution in one of the genes that encode H3.3: *H3-3B* (*H3F3B*) (> 95%) on chromosome 17 or, less frequently, *H3-3A* (*H3F3A*) on chromosome 1 […]. Among bone tumours, this is highly specific for chondroblastoma, although one case of clear cell chondrosarcoma was reported to harbour an *H3-3B* (*H3F3B*) p.Lys36Met mutation …	**Diagnostic molecular pathology** The vast majority of chondroblastomas harbour a p.K37M (K36M) substitution in one of the genes that encode H3.3: *H3-3B* (formerly *H3F3B*) (> 95%) on chromosome 17 or, less frequently, *H3-3A* (formerly *H3F3A*) on chromosome 1 […]. Among bone tumours, this is highly specific for chondroblastoma, although one case of clear cell chondrosarcoma was reported to harbour an *H3-3B* (formerly *H3F3B*) p.K37M (K36M) mutation …
Essential and desirable diagnostic criteria … *Desirable:* a fine network of pericellular chicken-wire calcification; presence of H3.3 mutation demonstrated by p.Lys36Met (K36M) expression or *H3-3A* (*H3F3A*) / *H3-3B* (*H3F3B*) mutation analysis.	**Essential and desirable diagnostic criteria** … *Desirable:* a fine network of pericellular chicken-wire calcification; presence of H3.3 mutation demonstrated by p.K37M (K36M) expression or *H3-3A* / *H3-3B* mutation analysis.

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Synovial chondromatosis (p. 368)

The ICD-O label has been corrected as shown.

Original text	Corrected text
ICD-O coding 9220/1 Chondromatosis NOS	**ICD-O coding** 9220/1 Synovial chondromatosis

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Osteoma (p. 391)

The ICD-O label has been corrected as shown.

Original text	Corrected text
ICD-O coding 9180/0 Osteoma NOS	**ICD-O coding** 9180/0 Osteoma

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Osteoid osteoma (p. 394)

The ICD-O label has been corrected as shown.

Original text	Corrected text
ICD-O coding 9191/0 Osteoid osteoma NOS	**ICD-O coding** 9191/0 Osteoid osteoma

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High-grade surface osteosarcoma (p. 417)

The text has been corrected as shown.

Original text	Corrected text
Pathogenesis The pathogenetic mechanisms of high-grade surface osteosarcoma are unknown. High-grade surface osteosarcomas arising in parosteal osteosarcomas (dedifferentiated parosteal osteosarcomas) display amplification of *MDM2* and *CDK4*. The single case of *TSPAN31* (*SAS*) amplification in a high-grade surface osteosarcoma heretofore described {2616} was an example of dedifferentiated parosteal osteosarcoma because it had grade 1 foci.	**Pathogenesis** The pathogenetic mechanisms of high-grade surface osteosarcoma are unknown. High-grade surface osteosarcomas arising in parosteal osteosarcomas (dedifferentiated parosteal osteosarcomas) display amplification of *MDM2* and *CDK4*. The single case of *TSPAN31* (*SAS*) amplification in a high-grade surface osteosarcoma heretofore described {2312A} was an example of dedifferentiated parosteal osteosarcoma because it had grade 1 foci.
References cited above: **2312A.** Noble-Topham SE, Burrow SR, Eppert K, et al. SAS is amplified predominantly in surface osteosarcoma. J Orthop Res. 1996 Sep;14(5):700–5. PMID:8893761 **2616.** Reul H, Eichler M, Potthast K, et al. In vitro testing of heart valve wear outside of the manufacturers laboratory–requirements and controversies. J Heart Valve Dis. 1996 Jun;5 Suppl 1:S97–103, discussion 103–4. PMID:8803761	

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Giant cell tumour of bone (p. 440)

The ICD-O label has been corrected as shown.

Original text	Corrected text
ICD-O coding 9250/1 Giant cell tumour of bone NOS	**ICD-O coding** 9250/1 Giant cell tumour of bone

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Giant cell tumour of bone (p. 440–446)

The following subsections have been corrected as shown.

Original text	Corrected text
Localization … Giant cell tumours in the axial skeleton arise most commonly in the sacrum and vertebral body […]; a tumour confined to the posterior elements only is not a giant cell tumour of bone. Flat bone involvement is rare but most frequent in the pelvis. Small numbers of giant cell tumours affect the tubular bones of the hands and feet …	**Localization** … Giant cell tumours in the axial skeleton arise most commonly in the sacrum and vertebral body […]; a giant cell tumour of bone is rarely confined to the posterior elements of the spinal vertebra. Flat bone involvement is rare but pelvic bones are most frequently affected. Small numbers of giant cell tumours occur in the tubular bones of the hands and feet …

Original text	Corrected text
Pathogenesis ***Conventional giant cell tumour*** … At least 95% of giant cell tumours harbour pathogenic *H3-3A* (*H3F3A*) gene mutations, approximately 90% of which are H3.3 p.Gly34Trp, with the next most common being p.Gly34Leu; rarer variants (p.Gly34Met, p.Gly34Arg, and p.Gly34Val) have also been reported …	**Pathogenesis** ***Conventional giant cell tumour*** … At least 95% of giant cell tumours harbour pathogenic *H3-3A* (*H3F3A*) sequence variants, approximately 90% of which are p.G35W (G34W), with the next most common being p.G35L (G34L); rarer variants (p.G35M [G34M], p.G35R [G34R], and p.G35V [G34V]) have also been reported …
Histopathology … ***Malignant giant cell tumour*** … The malignant component […]. In some cases of malignant transformation, the H3.3 p.Gly34 mutation, as demonstrated by immunohistochemistry, is retained in the malignant population […], but there is also evidence that expression of the H3.3 protein is absent in at least some cases […]. Finally, some bone sarcomas without associated giant cell tumour histology harbour an *H3-3A* (*H3F3A*) or *H3-3B* (*H3F3B*) p.Gly34 mutation […]. Therefore, there is a move to expand the definition of primary malignant giant cell tumour on the basis of an *H3-3A* (*H3F3A*) or *H3-3B* (*H3F3B*) p.Gly34 mutation {91}. … ***Immunohistochemistry*** H3.3 p.Gly34Trp (G34W) immunohistochemistry is a reliable surrogate marker for molecular analysis …	**Histopathology** … ***Malignant giant cell tumour*** … The malignant component […]. In some cases of malignant transformation, the H3.3 p.G35 (G34) sequence variant, as demonstrated by immunohistochemistry, is retained in the malignant population […], but there is also evidence that expression of the H3.3 p.G35 (G34) is absent in at least some cases […]. Finally, some bone sarcomas without associated giant cell tumour histology harbour an *H3-3A* (formerly *H3F3A*) or *H3-3B* (formerly *H3F3B*) p.G35 (G34) mutation […]. Therefore, there is a move to expand the definition of primary malignant giant cell tumour on the basis of an *H3-3A* (*H3F3A*) or *H3-3B* (*H3F3B*) p.G35 (G34) sequence variant {91,1827A}. … ***Immunohistochemistry*** H3.3 p.G35W (G34W) immunohistochemistry is a reliable surrogate marker for molecular analysis …
Diagnostic molecular pathology An *H3-3A* gene mutation is detected in the neoplastic stromal cell population in as many as 96% of giant cell tumours […]; 90% of these are represented by the H3.3 p.Gly34Trp mutation. The p.Gly34Leu mutation is much less frequent and is mostly found in tumours in the small bones of the hand, patella, and axial skeleton. There have also been occasional reports of p.Gly34Val, p.Gly34Arg, and p.Gly34Met […]. Failure to detect an H3.3 mutation should prompt testing for alterations in other osteoclast-rich lesions.	**Diagnostic molecular pathology** *H3-3A* gene mutation is detected in the neoplastic stromal cell population in as many as 96% of giant cell tumours […]; 90% of these are represented by p.G35W (G34W). The H3.3 p.G35L (G34L) sequence variant is much less frequent and is mostly found in tumours in the small bones of the hand, patella, and axial skeleton. There have also been occasional reports of H3.3 p.G35V (G34V), H3.3 p.G35R (G34R), and H3.3 p.G35M (G34M) […]. Failure to detect an H3.3 sequence variant should prompt testing for alterations in other osteoclast-rich lesions.

Original text	Corrected text
Essential and desirable diagnostic criteria … *Desirable:* Detection of H3.3 p.Gly34–mutated cells.	**Essential and desirable diagnostic criteria** … *Desirable:* Detection of cells with H3.3 p.G35 (G34) sequence alteration.
References cited above: **91.** Amary F, Berisha F, Ye H, et al. H3F3A (histone 3.3) G34W immunohistochemistry: a reliable marker defining benign and malignant giant cell tumor of bone. Am J Surg Pathol. 2017 Aug;41(8):1059–68. PMID:28505000 **1827A.** Leske H, Dalgleish R, Lazar AJ, et al. A common classification framework for histone sequence alterations in tumours: an expert consensus proposal. J Pathol. 2021 Jun;254(2):109–20. PMID:33779999	

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Conventional chordoma (p. 451)

The ICD-O label has been corrected as shown.

Original text	Corrected text
ICD-O coding 9370/3 Chordoma NOS	**ICD-O coding** 9370/3 Conventional chordoma

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Poorly differentiated chordoma (p. 456)

The ICD-O label has been corrected as shown.

Original text	Corrected text
ICD-O coding 9370/3 Chordoma NOS	**ICD-O coding** 9370/3 Poorly differentiated chordoma

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Fibrocartilaginous mesenchymoma (p. 470)

The ICD-O label has been corrected as shown.

Original text	Corrected text
ICD-O coding 8990/1 Mesenchymoma NOS	**ICD-O coding** 8990/1 Fibrocartilaginous mesenchymoma

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Rosai–Dorfman disease (p. 498)

The *ICD-O coding* subsection has been updated as shown.

Original text	Corrected text
ICD-O coding None	**ICD-O coding** 9749/3 Rosai–Dorfman disease

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Updated in print: Yes (in 3rd print run), December 2022

References (p. 572, 579)

Two new references have been added to the reference list:

1827A. Leske H, Dalgleish R, Lazar AJ, et al. A common classification framework for histone sequence alterations in tumours: an expert consensus proposal. J Pathol. 2021 Jun;254(2):109–20. PMID:33779999

2312A. Noble-Topham SE, Burrow SR, Eppert K, et al. SAS is amplified predominantly in surface osteosarcoma. J Orthop Res. 1996 Sep;14(5):700–5. PMID:8893761

Updated online: n/a – A standalone reference list is currently not included in the WHO Classification of Tumours Online
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References (p. 591)

A new reference has been added to the reference list:

3064A. Thiex R, Mulliken JB, Revencu N, et al. A novel association between RASA1 mutations and spinal arteriovenous anomalies. AJNR Am J Neuroradiol. 2010 Apr;31(4):775–9. PMID:20007727

Updated online: n/a – A standalone reference list is currently not included in the WHO Classification of Tumours Online
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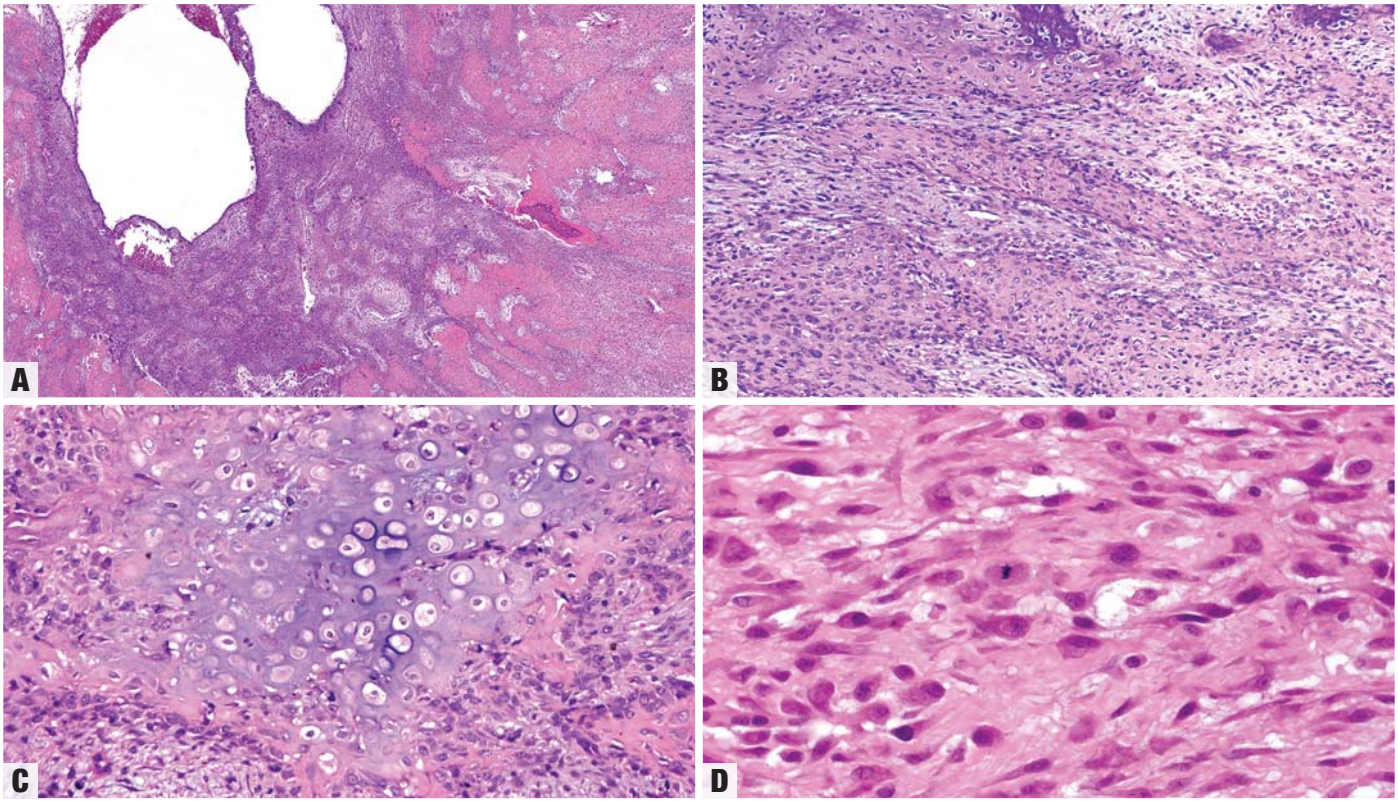

Fig. 1.58 Myositis ossificans. **A** Zonation pattern with focally cystic hypercellular centre surrounded by progressively maturing woven bone. **B** Poorly formed woven bone associated with osteoblasts merges with matrix that is well formed and trabecular in architecture. **C** Hypercellular hyaline cartilage undergoing enchondral ossification. **D** Fascicles of plump spindle cells with elongate nuclei that are mitotically active. The stroma is myxocollagenous with scattered extravasated red blood cells. Histological resemblance to nodular fasciitis is evident.

Etiology
Unknown

Pathogenesis
Most cases of myositis ossificans and FP harbour the fusion *COL1A1-USP6* {2980,3008,1036,260,1504}. *USP6* fusion genes are also encountered in aneurysmal bone cyst and nodular fasciitis, tumours with overlapping morphology.

Macroscopic appearance
Myositis ossificans is well delineated and ovoid, has a glistening soft-tan haemorrhagic centre and a firm greyish-white gritty periphery, and is 2–12 cm (average: 5 cm). FP is tan/grey/pink, smaller, and less well demarcated.

Histopathology
Myositis ossificans is characterized by zonal architecture. Initially, it is densely cellular, composed of spindle cells oriented randomly or in short intersecting fascicles. The spindle cells have eosinophilic cytoplasm and plump vesicular nuclei with nucleoli. Normal mitoses are often numerous. The stroma is vascular and myxoid and contains fibrin, extravasated erythrocytes, scattered lymphocytes, and osteoclast-like giant cells. Blood-filled cysts may be present. Peripherally, the spindle cells merge with osteoblasts that rim and populate ill-defined trabeculae and sheets of unmineralized woven bone, which is surrounded by well-formed trabecular and cortical-type bone that remodels into lamellar bone. Occasionally, the matrix contains cellular hyaline cartilage or the zonal architecture is not well developed {12,802,2116,2335,2658,2987}. The bone is randomly distributed in FP. An important differential diagnosis is extraskeletal osteosarcoma, which lacks zonation and shows malignant cytology.

Cytology
Cytology features a dual cell population of spindle cells and large ganglion-like cells set in a myxoid stroma {1649}.

Diagnostic molecular pathology
Molecular studies for *USP6* rearrangement may be useful in the appropriate clinicopathological context.

Essential and desirable diagnostic criteria
Essential: hypercellular fascicles of uniform spindle cells; admixed woven bone with zonation, being most mature at the periphery.

Staging
Not clinically relevant

Prognosis and prediction
Treatment of myositis ossificans and FP is usually simple excision. Prognosis is excellent; recurrence is uncommon.